Section 4

Respiratory system

15 Respiratory Distress

Respiratory distress occurs among 4-7% of all neonates[1,2] and is the reason for 30-40% of admissions in the NICU. It is more common among preterm (30%) and post term (21%) than among term neonates (4.2%).[2]

Definition

National Neonatal Perinatal Database of India (NNPD)[3] defines respiratory distress as presence of any two of the following features:

1. Respiratory rate (RR) >60/minute
2. Subcostal/intercostal recessions
3. Expiratory grunt/groaning

In addition to the above features, presence of nasal flaring, suprasternal retractions, decreased air entry on auscultation of the chest also indicates the presence of respiratory distress. Gasping, choking or stridor (signs of upper airway obstruction), apnea or poor respiratory effort or bradycardia, poor perfusion and cyanosis are life threatening signs that require prompt intervention.[4]

Causes

Respiratory distress in neonates can be due to a wide variety of conditions (Table 15.1). The frequency of a given condition depends on various factors of which gestation is an important one. In preterm neonates, respiratory distress syndrome (RDS) is the most common cause while in the late preterm and term neonates transient tachypnea of newborn (TTN) is the predominant cause.[2]

RDS due to surfactant deficiency has an overall incidence of 1.2% among all neonates in India and 40-50% among very low birth weight (VLBW) neonates. Other common causes of respiratory distress among VLBW neonates include sepsis or

pneumonia, transient tachypnea, air leak, patent ductus arteriosus etc. Among term inborn neonates born at various hospitals under the NNPD network, respiratory distress was noted in 4.4% of all live births and the etiologies were: TTN (46.7%), meconium aspiration syndrome (MAS, 29%), RDS (3.7%), pneumothorax (3.4%) and pneumonia (2.1%). Nineteen percent of them required mechanical ventilation and the overall case fatality rate (CFR) was 25%. However, among outborn neonates, 31% had respiratory distress, with pneumonia and MAS being the most common. Two thirds of outborn neonates with respiratory distress required mechanical ventilation and had higher CFR (38.5%).

Table 15.1: Common causes of respiratory distress

Airway	
	Choanal atresia
	Pierre Robin sequence
	Tracheoesophageal fistula
	Laryngo-tracheomalacia
	Vocal cord paralysis
Pulmonary Diseases	
	Transient tachypnea of the newborn
	Respiratory distress syndrome
	Meconium aspiration syndrome
	Pneumothorax
	Persistent pulmonary hypertension of the newborn
	Pulmonary hypoplasia
	Diaphragmatic hernia
Cardiac Diseases	
	Congenital heart disease
	Arrhythmia
	Congestive cardiac failure
	Cardiomyopathy
Thoracic Causes	
	Chest wall deformity
	Skeletal dysplasia
Neuromuscular Diseases	
	Central nervous system damage (birth trauma, hemorrhage, meningitis, asphyxia)
	Medication (maternal sedation, narcotic withdrawal)
	Muscular disease (myasthenia gravis)
	Spinal cord injury
Others	
	Sepsis
	Anemia
	Polycythemia

Hypo and hyperthermia

Initial assessment

Initial assessment of respiratory distress should be done to identify life threatening conditions, such as inadequate respiratory efforts or obstructed airway (gasping, choking, stridor) or circulatory collapse (bradycardia, hypotension, poor perfusion). If such features are present, emergency measures such as oxygen administration, bag and mask ventilation or intubation should be carried out as necessary.[4]

History

A detailed history is important in assigning a cause to the respiratory distress (Table 15.2).

Table 15.2: Relevant history in neonates with respiratory distress[6]

Antenatal

Maternal history of:

Diabetes mellitus: TTN, RDS, hypoglycemia, large for date

Pregnancy induced hypertension (PIH)

IUGR: Polycythemia, hypoglycemia

Asthma: TTN

Fever, UTI: Sepsis

Substance abuse: Narcotic drug withdrawal

Polyhydramnios: Tracheo esophageal fistula, neuromuscular disorders

Oligohydramnios: Pulmonary hypoplasia

Rh isoimmunization: Hydrops fetalis

Antenatal steroids status: RDS

Previous sibling with respiratory distress: Surfactant protein B deficiency

Intranatal

Prolonged rupture of membranes, intrapartum fever or chorioamnionitis: Sepsis

Meconium stained liquor: Meconium aspiration syndrome, asphyxia

Fetal distress: Asphyxia

C-section without labor: TTN, RDS, PPHN

Breech presentation, instrumental delivery: Trauma, Erb's with phrenic nerve palsy

Postnatal

Onset at birth: TTN, RDS, pneumothorax or air leak, MAS, congenital malformations

Onset hours or days later: Congenital heart disease, sepsis

General examination

Identify a clue to the etiology such as dysmorphic features, anomalies, features of intrauterine growth restriction, single umbilical artery, scaphoid abdomen, drooling of saliva, etc.

Assessment of respiratory distress

Inspection: Observe whether the neonate is breathing comfortably or if signs of respiratory distress are present. Note the respiratory rate, symmetry of chest excursions and synchrony with abdominal wall movement. Also note the color of the neonate (pink vs cyanosis) and use a pulse oximeter to determine the oxygen saturation. Note the shape of the chest wall- a rounded thorax with increased anteroposterior diameter is a marker of hyperinflation.

Some important respiratory signs are described below:

- **Tachypnea:** Count the RR for one full minute. Neonates with respiratory distress breathe at a faster rate to improve minute ventilation and gas exchange. Neonates with metabolic acidosis have deep, sighing breaths called Kussmaul's breathing as a compensatory mechanism.
- **Apnea or gasping efforts:** Preterm neonates with immature respiratory regulation, neonates with CNS depression due to various etiology and those in verge of respiratory failure manifest with apnea (cessation of breathing >20 s). This can be associated with bradycardia and/or cyanosis.
- **Nasal flaring:** Widening of ala nasi during respiration occurs to increase the cross-sectional area of the nostrils thereby reducing upper airway resistance.
- **Grunting:** This is an expiratory noise heard due to closure of the glottis during expiration. By this neonates can increase the intrinsic positive end expiratory pressure (PEEP) to prevent alveolar collapse during expiration and to maintain the functional residual capacity (FRC). This is especially helpful in preterm neonates with RDS. Grunting generally

disappears when the baby starts improving but it can also disappear in a neonate who is worsening because of exhaustion. Hence it has to be assessed in the context of other features such as oxygen saturation, color and activity of the neonate.

- **Retractions or chest recessions:** These indicate the use of accessory muscles of respiration. Intercostal retractions suggest parenchymal lung problem whereas suprasternal and supraclavicular recessions are noted with airway obstruction.
- **Stridor:** It is a harsh "crowing" sound produced due to narrowing of the upper airways at the level of larynx or extra thoracic trachea. It is often inspiratory but can be expiratory or biphasic. Stridor can occur due to laryngomalacia, Pierre Robin sequence, vocal cord palsy, laryngeal or subglottic narrowing due to edema, web or stenosis.[5]
- **Stridor:** This is a low pitched inspiratory noise produced as a result of obstruction at the level of nasopharynx (adenoid hypertrophy) or oropharynx (micrognathia, macroglossia). This sound can be inspiratory, expiratory or both.
- **Wheezing:** This is a musical expiratory sound produced by narrowing of small airways (bronchioles). It is better appreciated with a stethoscope.

One can differentiate the site (upper airway: extrathoracic or intrathoracic; or lower airway) and type of obstruction (fixed or variable) in the tracheobronchial tree based on the various respiratory sounds and their relation to respiration (Table 15.3).

Table 15.3: Respiratory sounds in relation to the site of airway obstruction[5]

Site of obstruction		Type of sound and its mechanism	Causes
Upper airway	Supra-glottic area including epiglottis	Inspiratory stridor.	Laryngomalacia, laryngocoele, laryngeal hemangioma or mass due to inflammation, infection or trauma
	Glottis	Stridor tends to be inspiratory or biphasic and often fixed	Vocal cord palsy. If unilateral, the stridor is generally inspiratory and if bilateral it is biphasic and fixed.
	Sub-glottis	Biphasic and fixed stridor	Obstruction due to inflammation, trauma, hemangioma, edema or foreign body
	Trachea	Fixed obstruction (stenosis): Biphasic stridor Variable (e.g. foreign body), intra-thoracic obstruction: Expiratory stridor Variable, extra thoracic tracheal Inspiratory stridor.[6]	Tracheomalacia, foreign body, vascular rings, stenosis, inflammation
Lower airway	Bronchi, bronchioles	Wheezing; better heard with a stethoscope	Bronchospasm, BPD, asthma, airway narrowing due to edema

Palpation and percussion: While palpation and percussion are done sparingly in neonates, one can get valuable information by feeling the tracheal position, locating the apex beat, palpating for crepitus or murmurs and percussing for normal resonance. Dullness on percussion may be noted over areas of

consolidation or collapse, stony dullness over pleural effusion and hyper-resonance over pneumothorax or bulla.

Auscultation: Assess whether the breath sounds are heard equally and symmetrically in all areas, whether there is prolongation of inspiratory or expiratory phase, and presence of added sounds like rales, rhonchi, wheeze and stridor.

Cardiac examination: Examination of respiratory system is incomplete without examination of cardiac system. Neonates with cardiac disease manifest tachypnea without significant retractions, may have poor perfusion, cyanosis and abnormal heart sounds or murmurs on auscultation. Pulse rate, blood pressure and capillary refill time should also be monitored to identify hypoperfusion, which can be secondary to prolonged hypoxemia.

Respiratory distress score: In order to objectively grade the severity, the signs of respiratory distress are assigned a numerical score (0 indicating best score in the category and 2 indicating the worst) and individual scores are combined to produce a final respiratory distress score. The final score is classified into mild (<5), moderate (5-7) and severe (>7)to indicate the severity of distress. The two commonly used respiratory distress scores are the Silverman Anderson score[7] (Figure 15.1) and Downes' Vidyasagar Score[8] (Table 15.4). The advantages of these scores are that they provide objective means of quantifying respiratory distress, help to follow the progression of distress over time as well as to initiate treatment. Neonates with mild distress but with cyanosis can be managed with oxygen delivery devices (oxygen hood or nasal prongs), those with moderate distress need positive distending pressure like CPAP while those with severe distress need intubation and mechanical ventilation. They are simple and can be easily used by nurses.[9] The Silverman Score had good correlation with mortality and the Downes' score had good correlation with physiological parameters like arterial pH and blood-gas as well as mortality.

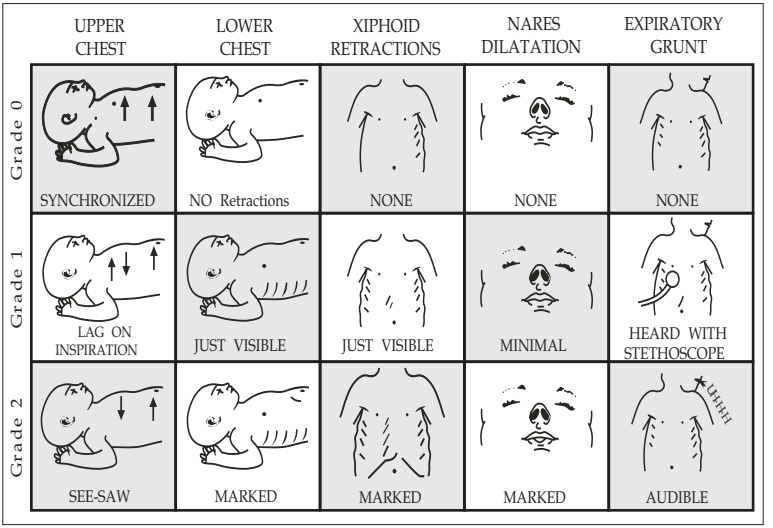

Figure 15.1: Silverman Anderson score [7]

Upper chest movement: Upper chest is the part of the chest anterior to the mid axillary line. Upper chest movement is assessed by observing the synchrony of the movement upper chest with abdomen. *Lower chest retractions:* are assessed by observing the retractions between the ribs below the mid axillary line. *Xiphoid retractions:* Retraction below the xiphoid process are rated as none, minimal or marked. *Nasal flaring*: Normally, there should be no nasal *flaring*. *Expiratory grunting*: Grunting that is audible with a stethoscope is scored '1', and grunting that is audible without using a stethoscope is scored 2. A score greater than 7 indicates that the baby is in respiratory failure.

Table 15.4: Downe's score for grading severity of respiratory distress

Feature	Score 0	Score 1	Score 2
Cyanosis	None	In room air	In 40% FiO_2
Retractions	None	Mild	Severe
Grunting	None	Audible with stethoscope	Audible without stethoscope
Air entry	Normal	Decreased	Barely audible
Respiratory rate	<60	60-80	>80 or apnea

Oxygen saturation

Pulse oximeter is an important device that can measure the oxygen saturation, often referred to as the sixth vital sign. The oxygen saturation below 90% indicates hypoxia.[10] It should be checked both in pre-ductal (right hand) and post-ductal sites (leg). A pre-postductal difference of more than 5% to 10% indicates probable right-to-left shunt through PDA in the setting of PPHN. Central cyanosis is an important indicator of hypoxia. The level of deoxy-hemoglobin should be least 2.5 g/dL in the blood to manifest cyanosis. Polycythemic infants with high hemoglobin may manifest cyanosis when oxygen saturation is 88% while anemic neonates may not appear cyanosed until saturation drops below 65%[11]. Peripheral cyanosis can be due to cold exposure or polycythemia but can also be a manifestation of potentially serious conditions like hypoglycemia, sepsis or decreased left ventricular output like hypoplastic left heart syndrome or coarctation of aorta.

Approach to management

Specific management depends on the underlying condition and a diagnosis can be established in most by reviewing the history, clinical examination and use of necessary investigations (Table 15.5).

Investigations

The following are some of the common investigations that are performed in a neonate with respiratory distress. The selection of tests depends on the clinical condition, availability and

Table 15.5: Differential diagnosis of respiratory distress

Condition	Risk factors	Clinical course	Radiological features
Respiratory distress syndrome (RDS)	• Prematurity (usually <34 weeks) • Lack of antenatal steroids • Infant of diabetic mother • Birth asphyxia • Rh isoimmunization	• Onset at or soon after birth • Progresses till 48 hrs, static for 48 hrs and improves later (surfactant therapy modifies this course with earlier resolution of the disease) • FiO_2 requirement often more than 40%	• Low volume lungs (may not be seen in a baby receiving CPAP therapy or mechanical ventilation). • Fine reticulo-granular pattern- Ground glass appearance • Air bronchograms • White- out lungs
Transient tachypnea of newborn (TTN)	• Predominantly late preterm and term infants • Born by Caesarean section • Maternal diabetes	• Onset at or soon after birth • Maximum severity at birth and improves gradually • FiO_2 requirement generally not more than 40%	• Hyperinflated lungs • Perihilar streaking • Fluid in minor fissure • Pleural effusion • Mild cardiomegaly
Early onset sepsis (EOS)/ pneumonia	• Risk factors such as PROM, chorioamnionitis, maternal fever, unclean vaginal examinations	• Onset at birth or delayed • May fail to improve with oxygen/ CPAP	• Homogeneous/ heterogenous opacities bilaterally
Meconium aspiration syndrome (MAS)	• Meconium stained amniotic fluid	• Onset may be at birth or delayed • Meconium staining of cord/ skin • Hyperinflated chest • Features of PPHN	• Hyperinflated lungs • Coarse nodular opacities • Patchy atelactasis • Areas of overinflation

whether a particular test would be useful in the given scenario. For example, in a neonate with suspected tension pneumothorax, it would be wise to do a trans-illumination of thorax and proceed with treatment rather than wait for a chest x ray.

1. **Gastric aspirate shake test:** Shake test is a simple bedside test that can be done to predict the risk of RDS and is especially useful in units where bedside radiography is unavailable. The test involves mixing 0.5 mL of gastric aspirate obtained within one hour of birth with equal volume of 95% ethyl alcohol in a clean glass test tube (4 mL glass tube of 82×10.25 mm). The tube is corked, shaken for 15 seconds and left to stand for 15 minutes before the liquid- air interface is examined for the stability of bubbles.[12] Presence of an entire rim of bubbles is considered a positive test, while absence of bubbles is negative and incomplete rim of bubbles is an intermediate test. The test is highly specific but has a sensitivity of only 70%. In one study, none of the infants with a positive test developed RDS while 66% of those with a negative test result developed RDS.[13]
2. **Transillumination:** A fiber-optic bright light source applied to the chest wall can be used to to promptly identify air leaks like pneumothorax. Severe PIE and emphysematous bullae may also trasilluminate. The room must be dark while performing this test and one must differentiate the small normal halo of light around the probe from increased transillumination noted from air collection.
3. **Chest radiography:** Radiography is the main diagnostic tool for respiratory distress. The commonly taken view is antero-posterior while lateral and cross-table lateral views can be done for evaluation of air leaks, pleural effusions and placement of tubes or catheters (see the chapter on chest radiograph).
4. **Ultrasound:** Ultrasonography can be used to evaluate pleural and pericardial effusions, detection of pneumothorax, evaluation of mediastinal and thoracic masses, assess the position and movement of diaphragm as

in eventration and diaphragmatic palsy, and confirm the position of intravascular catheters.

5. **Arterial blood gas analysis (ABG):** ABG provides a snapshot information about the respiratory condition:
   a. Normal values are pH 7.35-7.45, PaO_2 50-80 mmHg, $PaCO_2$ 35-45 mmHg, bicarbonate 20-24 mEq/L and base deficit of 3-5 meg/L.
   b. **Respiratory failure** is present when there is hypoxemia (PaO_2 <50), hypercarbia ($PaCO_2$ >60), and acidosis (pH<7.2).
   c. Hypoxemia may result from both cardiac and respiratory causes
   d. Hypercarbia is a better indicator of respiratory failure. Rising $PaCO_2$ ($PaCO_2$ >60) in the presence of falling pH (pH <7.25) denotes failure of gas exchange and indicates the need for mechanical ventilation.
   e. The goal of ventilation is not to make the blood gases entirely normal but to keep them within acceptable target ranges.
6. **Oxygenation indices:** These indices give an idea about the severity of respiratory illness and are useful in instituting therapy as well as predicting death and adverse respiratory outcome. The three commonly used oxygenation indices are
   a. Alveolar-arterial oxygen pressure difference (A-a DO_2).

   This can be calculated using the formula: $AaDO_2 = (713 \times FiO_2) - (PaCO_2 / 0.8) - (PaO_2)$, where 0.8 indicates respiratory quotient on a mixed diet and 713 is derived from 760 mm Hg (atmospheric pressure at sea level)- 47 mmHg (alveolar water vapor pressure). In healthy infants $AaDO_2$ is less than 20 in room air. In the face of hypoxia, if $AaDO_2$ is normal, it indicates alveolar hypoventilation or low inspired FiO_2. If $AaDO_2$ is increased, it may be because of ventilation-perfusion (V/Q) mismatch or shunt. If one were to increase the FiO_2 to 100% and observes an increase in PaO_2 then V/Q mismatch might be operating while no change in PaO_2

means shunt. The normal $AaDO_2$ is highly dependent on FiO_2 (for each 10% increase in FiO_2, AaDO2 value increases by 5-7 points) and so the value should not be interpreted without the FiO2.

b. **Arterial-to-alveolar oxygen tension ratio (a/A ratio):** The a/A ratio should be close to 1 in a healthy infant. A ratio of less than 0.3 indicates disturbances in oxygen transfer.

c. **Oxygenation index:** OI = [mean airway pressure X FiO_2/PaO_2(mmHg)] X 100. An OI > 15 indicates ventilation-perfusion mismatch and OI 40 is associated with a very poor prognosis with mortality approaching 80%. Infants with hypoxic respiratory failure and OI>25 may benefit from inhaled nitric oxide (iNO) and when OI exceeds 40, ECMO therapy is indicated.

While any of the 3 indices can be used, OI is said to be a very sensitive indicator of severity of respiratory illness because it factors in the pressure cost of achieving oxygenation, namely MAP.

7. **Other investigations:** Sepsis screen and blood cultures are indicated when infection is suspected. Blood sugars and electrolytes should be monitored. CSF examination is warranted in the presence of clinical sepsis or positive blood culture. Echocardiography should be done to rule out congenital heart disease and to evaluate PPHN.

Treatment

The basic principles of treatment include

- **Supportive care:** This includes maintenance of thermo-neutral environment by caring the infant under radiant warmer or in an incubator, ensuring normal blood glucose levels with enteral and/or parenteral nutrition, and monitoring vital parameters such as heart rate, respiratory rate, SpO_2 and CFT. Documenting the respiratory distress score serially helps to early identification of worsening.
- **Respiratory support:** Respiratory support provided to the

infant depends on many factors such as severity of respiratory distress, hemodynamic stability, presence of spontaneous efforts, the underlying condition and the presence of complication if any. The objective is to ensure adequate oxygenation and ventilation, and thereby decrease the work of breathing.

- **Monitoring for and management of complications:** Infants with respiratory distress need to be monitored for worsening of the distress, hemodynamic instability, features of PPHN, acute kidney injury due to hypoxia and complications due to mechanical ventilation. If any such complications develop, they should be managed appropriately.

Principles of respiratory management in common conditions

Respiratory distress syndrome

- Very low birth weight neonates at risk for RDS can be supported with CPAP in the delivery room and continued in the NICU. Early institution of CPAP has been shown to decrease the need for ventilation.[14]
- In the NICU, preterm neonates with good spontaneous respiratory efforts but manifesting respiratory distress should be started on nasal CPAP at 5 cm H_2O and titrated FiO_2 to achieve target SpO_2 between 90-95%. If FiO_2 requirement exceeds 40%, early rescue surfactant by InSurE technique is indicated. Early use of CPAP in infants with respiratory distress reduces mortality, need for mechanical ventilation and surfactant (see surfactant protocol).[15]
- Intubation and mechanical ventilation can be initiated if there is hypercapnia (PCO_2 >60 mmHg), decreased respiratory drive or acidosis or if surfactant replacement therapy is planned.

Transient tachypnea of newborn (TTN)

- Treatment of TTN is mainly supportive. The symptoms generally resolve within 1 to 5 days after minimal therapeutic intervention.

- Respiratory support may involve oxygen therapy while some may require CPAP to distend the alveoli and aid the absorption of the extra lung fluid. Very rarely mechanical ventilation is necessary.

Meconium aspiration syndrome

- Intrapartum care: Routine oropharyngeal suction and endotracheal suctioning are to be avoided in neonates born through meconium stained liquor. NRP recommends that even non-vigorous neonates (depressed respirations or poor muscle tone) should proceed through initial steps; positive pressure ventilation should be provided if apneic or heart rate is < 100/ min. [16]
- Postnatal management: Infants who develop respiratory distress should be admitted to NICU. Repiratory support may involve oxygen delivered via hood or canula or CPAP, if FIO_2 requirement exceeds 40%.
- Mechanical ventilation should be considered when infants with MAS demonstrate significant hypoxia (PaO2 <50mmHg) , hypercarbia (PaCO2 >60mm Hg), or acidosis (pH <7.25) with FiO2 >0.80.[17] Surfactant therapy decreases the need for extracorporeal membrane oxygenation (ECMO) therapy in MAS but not mortality or other clinical outcomes.[18] In severe cases with hypoxemic respiratory failure, early institution of high frequency ventilation along with iNO therapy may decrease the use of ECMO and improve outcomes.[19]

Pneumonia

Management is supportive and includes oxygen therapy, appropriate respiratory support, antibiotics, and vasopressors such as dopamine and dobutamine if there is shock.

Air-leak syndromes

- Spontaneous pneumothorax is noted in 1% of term neonates but only 10% of them manifest symptoms. Pneumothoraces complicating respiratory conditions like MAS, congenital bullae, pneumonia, pulmonary hypoplasia and interventions like CPAP or mechanical ventilation are often

symptomatic.

- Nitrogen washout (administering 100% oxygen by hood or prongs) for 12-24 hours used for small symptomatic pneumothoraces has not been shown to be beneficial.[20] This technique is not recommended now.
- Needling the chest in the second or third intercostal space in the mid-clavicular line using a butterfly needle, 3 way stop-cock and a syringe can be used to treat a small symptomatic pneumothorax in neonates who are not mechanically ventilated and as a temporary measure in those who are mechanically ventilated.
- Neonates who are mechanically ventilated and develop a pneumothorax require chest tube for continuous drainage as the air-leak may be persistent.
- PIE (pulmonary interstitial emphysema) is one form of pulmonary air leak syndrome that occurs in ventilated preterm neonates with RDS. PIE results in carbon dioxide retention, hypoxia and respiratory acidosis. Chest x-ray aids in diagnosis. Management involves minimizing the barotrauma by decreasing PIP, adjusting PEEP to maintaining sufficient FRC and targeting acceptable blood gases and permissive hypercapnia. High frequency ventilation (jet ventilation preferably) can help in early resolution of PIE by providing ventilation at lower mean air way pressure. Supportive care involves maintaining hemodynamic status, adequate oxygenation and nutritional support.

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